examining the oligonucleotide primers in the specification and reading the description on page 16, lines 24-33 will recognize the very similar GC base pair ratio and the importance of having similar base pair ratios. Support for using more enzyme can be found on page 17, line 12 where it is shown that the Taq polymerase is added to achieve a final concentration of 100 units/mL. One skilled in the art would readily recognize that this is significantly higher in the levels in the literature as well as in the recommended levels in the brochures from Cetus (about 20-30 units/mL). On page 17, line 25-29, the times and temperatures for the reaction are given. These times are longer than those of the recommended times by the Cetus in their advertisement and sales brochures. One skilled in the art would readily recognize the importance of the conditions shown in the specification.

Similarly, the specification shows that multiple PCR with about 25 cycles gives adequate results. However, one skilled in the art would readily recognize that the number of cycles can be increased or decreased to remove any ratio distortion which is observed. Thus, applicants have provided support in their original specification for the four elements which were shown to be recognized as important in the multiplex PCR assay.

In light of the comments and the affidavits, Applicants respectfully request that the § 112 rejection as to claims 1-5 and 7 be withdrawn.

Claims 6-8 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite. Claims 6-8 have been amended to remove the indefiniteness. The sequence in the claims now corresponds to the sequence in the specification. In light of the amendments, Applicants respectfully request withdrawal of this rejection.

Applicants respectfully request that reference DD be considered. Applicants assert that the reprint and cite are the same. The only difference between the copy of the reprint produced and that of the cite is that it eliminates the reference to the symposium which the paper came from. A new form 1440 with the new cite is submitted herewith.

Applicants do not believe any additional fees are due in this response. However, if any additional fees are due, please withdraw such fees from Account No. 06-2305 from which the undersigned is authorized to draw.

The amendments and remarks provided herein demonstrate that the specification is enabled and that there is adequate invention to support patentability. Accordingly, it is respectfully submitted that this application is now in condition for allowance.

If, however, any issues remain, the Examiner is respectfully requested to contact the undersigned at (713) 651-5325 to discuss the resolution of the outstanding issues.

Respectfully submitted,

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Human Genetics

Clinical case reports

Partial trisomy of the distal segment of 14q

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Summary. The case of a male infant with duplication of the distal segment of chromosome 14q is described. There was an extra chromosomal segment at the distal end of the long arm of chromosome 17. Banding techniques suggested that the extra segment might be the distal segment of chromosome 14q. DNA analysis using probes from distal 14q as well as from other parts of the genome confirmed that the extra segment consisted of the distal part of 14q. Both the proband's parents and his elder sister had normal karyotypes.

Introduction

Since Allerdice et al. (1971) first reported a case of partial trisomy 14q, a number of similar cases have been reported (Raoul et al. 1977). The trisomic segment was limited to the proximal part of chromosome 14q in most cases; mostly pter to q11–q24 (Young et al. 1976; Pajares et al. 1979). Cases of partial trisomy of the distal part of 14q have been described more recently (Turleau et al. 1983; Markkanen et al. 1984).

The present report describes a case of distal trisomy 14q, which was confirmed by the Southern blot method using a DNA probe derived from the distal segment of 14q.

Case report

The male infant described is the third child of healthy and nonconsanguineous parents. His elder sister was 3 years old and healthy at the time of his birth. The mother was 23 years old at the time of delivery. The baby was born full term and weighed 2502 g at birth. Turbid amniotic fluid was noticed at the delivery. The Apgar score was 7 points at 1 min after birth. The following physical features were noted at birth: protruding occiput, deformed ears, large face, a broad base of the nose, thin eyebrows, Mongoloid slant of eyes, a fistula located in the right preauricular region, protruding maxilla, wide sagittal suture, hypertelorism, high arched palate, abnormal teeth (two incisors) in the mandible (Fig. 1), whorl pattern on all the left fingers, no simian creases and no distal axial triradius by dermatoglyphic study, and hypospadia (Fig. 2). On admission, cyanosis and heart murmurs indicated congenital heart disease and chest roentgenography showed cardiac dilatation (cardiothoracic ratio 67%). Electrocardiography and echocardiography revealed hypertrophy of the right ventricle and a small patent ductus arteriosus. Cranial computed tomography showed no abnormality.

The patient has since been well except for poor weight gain. At 18 weeks, his weight was 4200 g (below 3rd percentile).

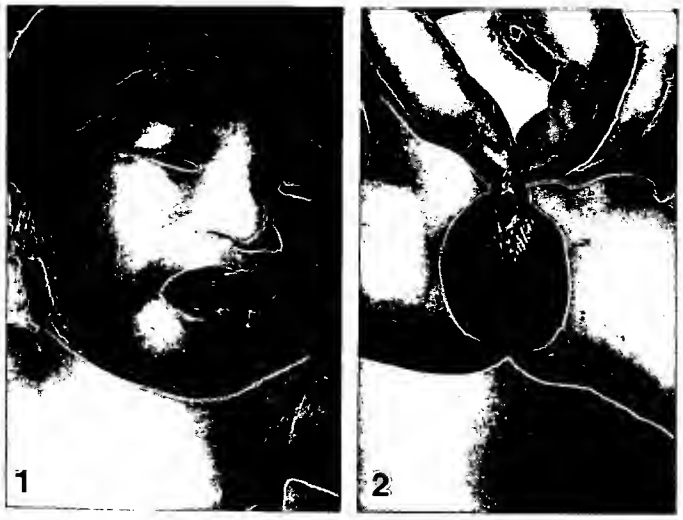

Fig. 1. The patient on the first day of life showing a broad base of the nose, thin eyebrows, Mongoloid slant of eyes, hypertelorism, protruding maxilla and abnormal teeth in the mandible

Fig. 2. Hypospadia

Cytogenetic studies

Metaphases were obtained by the standard lymphocyte-culture technique and examined by banding techniques including G-banding and R-banding with acridine orange stain.

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